ARUP LABORATORIES
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Tracy I. George, MD, Chief Medical Officer

Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	3/25/2020
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Angelman Syndrome and Prader-Willi Syndrome by Methylation-Sensitive PCR

ARUP test code 2005077

Angelman and Prader-Willi Specimen	Whole Blood
Angelman and Prader-Willi Result	Negative

Methylation pattern: Normal

Both the maternally and paternally contributed Angelman Syndrome (AS)/Prader-Willi Syndrome (PWS) critical regions are present in this sample. This result reduces, but does not exclude, a diagnosis of AS. Approximately 20 percent of individuals with AS will have normal methylation patterns. Within that group, approximately half will have UBE3A causative mutations, 1 percent will have a cytogenetically visible chromosomal rearrangement and the remainder (approximately 10 percent) will have an unidentified genetic mechanism. This result greatly reduces the chance for PWS, since 99 percent of individuals with PWS have abnormal methylation patterns.

Recommendations: Medical screening and management should rely on clinical finding and family history. A genetics consultation is recommended.

This result has been reviewed and approved by [redacted]

H=High, L=Low, *=Abnormal, C=Critical

BACKGROUND INFORMATION: Angelman Syndrome and Prader-Willi Syndrome by Methylation

CHARACTERISTICS OF ANGELMAN SYNDROME (AS): Developmental delays by 6-12 months of age, seizures, microcephaly, movement or balance disorder, minimal or absent speech, and a distinctive behavioral phenotype, which includes a happy demeanor with frequent laughter, hand flapping, and excitability.
PREVALENCE: 1 in 15,000.
INHERITANCE: Varies, depending on the molecular genetic mechanism.
CAUSE: Absence of maternal expression of the UBE3A gene.
MOLECULAR GENETIC MECHANISMS: Microdeletions in the AS/PWS critical region (68 percent), UBE3A mutations (11 percent), paternal uniparental disomy of chromosome 15 (7 percent), imprinting center defects (3 percent), unbalanced chromosome translocation (less than 1 percent), and unknown (10 percent).
Clinical Sensitivity: 78 percent.
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
METHODOLOGY: Bisulfite conversion and PCR amplification to detect methylation using melting curve analysis.
LIMITATIONS: Molecular mechanisms not affecting methylation patterns that may result in AS will not be assessed. Diagnostic errors can occur due to rare sequence variations.

CHARACTERISTICS OF PRADER-WILLI SYNDROME (PWS): Neonatal hypotonia, hyperphagia, obesity, global developmental delay, mild intellectual disability, hypogonadism, and a distinctive behavioral phenotype, which includes temper tantrums, stubbornness, manipulative behavior, and obsessive-compulsive behavior.
PREVALENCE: 1 in 15,000.
INHERITANCE: Varies, depending on the molecular genetic mechanism.
CAUSE: Absence of the paternally contributed PWS/AS critical region of chromosome 15q11.2-q13.
MOLECULAR GENETIC MECHANISMS: Microdeletions in the PWS/AS critical region (70-75 percent), maternal uniparental disomy of chromosome 15 (25-29 percent), imprinting center defect or balanced chromosome translocation (less than 1 percent).
CLINICAL SENSITIVITY: Over 99 percent.
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
METHODOLOGY: Bisulfite conversion and PCR amplification to detect methylation using melting curve analysis.
LIMITATIONS: Molecular mechanisms not affecting methylation patterns that may result in PWS will not be assessed. Diagnostic errors can occur due to rare sequence variations.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Angelman and Prader-Willi Specimen	20-094-400102	4/3/2020 4:54:00 AM	4/4/2020 4:51:19 AM	4/8/2020 3:15:00 PM
Angelman and Prader-Willi Result	20-094-400102	4/3/2020 4:54:00 AM	4/4/2020 4:51:19 AM	4/8/2020 3:15:00 PM

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical